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SYNTHEGO CORPORATION

UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

SAN JOSE DIVISION

SYNTHEGO CORPORATION,

Plaintiff/Counter-Defendant,

v.

AGILENT TECHNOLOGIES, INC.,

Defendant/Counter-Claimant.

Case No. 5:21-cv-07801-EJD

SYNTHEGO'S OPPOSITION TO AGILENT'S MOTION FOR A PRELIMINARY INJUNCTION

Judge: Judge Edward J. Davila

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I. INTRODUCTION

The facts here are the exact opposite of the emergency circumstances that might justify the extraordinary remedy of a preliminary injunction. Rather than being the first, or even an early, market entrant, Agilent entered the CRISPR guide RNA market long after Synthego and numerous other companies had already done so. Rather than promptly seeking injunctive relief when Synthego launched in 2016, Agilent stood on the sideline with its patent in hand for nearly ***three years*** before bringing this motion. Rather than notify Synthego of its desire for exclusivity promptly, Agilent welcomed Synthego to license its patent rights when it finally approached Synthego last year. By failing to act diligently, and then seeking to license its patents to the industry, Agilent effectively admits that it does not need an injunction and that normal money damages will suffice, even if it could prove entitlement to any relief.

On that note, there is a good explanation for Agilent's lackadaisical patent enforcement: The validity of its patents are, to the say the least, in serious doubt. Thus, Agilent cannot prove the likelihood of success necessary to justify a preliminary injunction. Well before Agilent even bothered to file the instant motion, Synthego filed two thorough petitions for *inter partes* review seeking to invalidate Agilent's patents. While the PTAB normally takes about 3 months to institute an IPR after receiving a preliminary response, in this case it did so after only about a month. It swiftly found that Synthego had shown a reasonable likelihood of proving that ***every single*** claim of Agilent's patents was invalid in view of the prior art and that every claim asserted in Agilent's injunction motion was ***anticipated*** by the prior art. IPRs. *See* Exs. 1-2. The PTAB found the key anticipation ground in Synthego's IPRs is "particularly strong":

> On the current record, we determine that the merits of Petitioner's anticipation ground appear to be ***particularly strong*** for the independent claims and for those dependent claims where Petitioner's arguments are similarly premised on the crRNA examples in Table 8 being anticipatory without any further modification.

Ex. 1 at 18; Ex. 2 at 18 (same).[1] Given the PTAB's decision, there are serious questions as to the validity of Agilent's patents, and it is difficult to understand why Agilent even maintains this motion.

[1] Emphases supplied throughout this brief.

To the extent Agilent even contends there are sales that might fall outside the market segment where it has offered Synthego a license, those sales are for the purpose of critical pre-clinical and clinical studies to seek FDA approval for new clinical products, including medicines and diagnostics. As such, these sales are not even infringing pursuant to the safe harbor of 35 U.S.C. § 271(e)(1) and cannot justify injunctive relief.

Agilent should know better than to pursue this motion. In *Waters Corp. v. Agilent Techs. Inc.*, 410 F.Supp.3d 702, 714-15 (D. Del. 2019), Agilent successfully defeated a preliminarily injunction motion, where, as here, the plaintiff was not diligent in pursuing injunctive relief, the patents were likely invalid in view of the prior art, and there was a strong public interest in ensuring adequate supply for clinical drug trials. Virtually every successful argument Agilent recently made in the *Waters* case—which Agilent tellingly does not address—confirms that an injunction is not warranted here. As documented below, there is no reason to depart from Agilent's own logic in the *Waters* decision and its motion should be denied.

II. LEGAL STANDARD

"A preliminary injunction is an extraordinary remedy never awarded as of right." *Winter v. Nat. Resources Def. Council, Inc.*, 555 U.S. 7, 24, (2008). "A plaintiff seeking a preliminary injunction must establish [1] that he is likely to succeed on the merits, [2] that he is likely to suffer irreparable harm in the absence of preliminary relief, [3] that the balance of equities tips in his favor, and [4] that an injunction is in the public interest." *Id.* at 20.

III. ARGUMENT

A. Agilent Has No Likelihood Of Success

A "likelihood of success on the merits" "is not shown if an alleged infringer raises a substantial question regarding either infringement or validity of the asserted patents." *Takeda Pharms. U.S.A., Inc. v. West-Ward Pharm. Corp.*, 785 F.3d 625, 630 (Fed. Cir. 2015). In fact, as Agilent has successfully argued, even if a patentee establishes a high likelihood of success on infringement, injunctive relief is still not warranted if there remains a substantial question on invalidity. *See Waters*, 410 F.Supp.3d at 713.

1. The Asserted Patents Are Invalid In View Of The Prior Art And There Is At Least A Substantial Question On Invalidity

At a minimum, there is a substantial question of invalidity precluding a finding of likelihood of success on the merits. *See Takeda*, 785 F.3d at 630. According to Agilent, it supposedly invented "synthetic chemically modified gRNAs…with specific chemical modifications of nucleotides that provide identifiable advantages over unmodified gRNAs…." Dkt. No. 39-3 at 5. Agilent filed its patents on this alleged invention in December 2014 and then, as Agilent alleges in its brief, published the work six months later in an article (the "Hendel paper") in the journal Nature Biotechnology. *Id*. at 6. In the Hendel paper, however, the inventors admitted that they did not actually invent any new modifications for RNA, but instead adopted known modifications from the prior art:

> We selected these modifications for evaluation owing to their previously reported stability to serum and snake venom phosphodiesterases and for their reported effects on the immunostimulatory properties of nucleic acids.

Dkt. No. 24-7 at 985. In fact, it was standard practice in the RNA field to use such chemical modifications for various purposes, and numerous different research groups had proposed to do precisely this in connection with CRISPR guide RNAs long before the Agilent inventors. Applying this standard technique to the newly-developed CRISPR platform epitomizes the type of non-inventive application of a known solution that is unworthy of a patent monopoly.

Accordingly, from the outset of this case, Synthego has informed Agilent that its patents are invalid in view of the prior art, making clear in its October 2021 declaratory judgment complaint that it planned to file IPRs challenging the validity of the patents. *See* Dkt. No. 1 at 1 n.1. Synthego subsequently moved with unusual diligence to do so, filing two comprehensive IPR petitions two weeks before Agilent even filed the instant motion. Those IPRs—which Agilent barely addresses in its brief—have quickly been instituted by the PTAB after review of Synthego's petitions and Agilent's response. As such, undeniably there is a substantial question as to the validity of Agilent's patents that precludes injunctive relief. Likewise, while Agilent glosses over Synthego's unenforceability arguments, after only limited discovery it has only become clearer that Agilent did not fulfill its duty of candor to the Patent Office when it failed to disclose the very prior art that it identified in the Hendel paper as teaching

the allegedly novel chemical modifications in its claims. This represents yet another basis to reject Agilent's motion.

a. The PTAB's Institution Decisions Preclude Injunctive Relief

As set forth in Synthego's IPR petitions, the patents-in-suit are invalid in view of the prior art. *See* Exs. 3 - 4. Although Agilent was well aware of Synthego's IPRs before seeking injunctive relief, it presents no response on the merits—and should not be able to save such a response for reply. Agilent fails to identify even a single claim element in any asserted claim that is supposedly absent from the anticipatory prior art identified in Synthego's IPRs. Ignoring the substance, Agilent's main response in its injunction motion to Synthego's IPRs is procedural. Specifically, Agilent contends that the PTAB is "highly unlikely" to institute the IPRs because the primary reference in the IPRs, Pioneer Hi-Bred, was listed in an information disclosure statement during prosecution among dozens of other references. Dkt. No. 39-3 at 19.

Agilent's litigation positions about the invalidity of its patents has proven unreliable. Agilent's predictions about what the PTAB would do were dead wrong. On April 26, Agilent filed its response to the institution of Synthego's IPRs, setting forth presumably its best rebuttal, including through 58-pages worth of expert witness testimony. While the PTAB was entitled to use three months to review Agilent's arguments and issue its institution decisions, remarkably it took just over a month to grant institution in this case. In its institution decisions, the PTAB concluded that Synthego had shown a reasonable likelihood that every single claim asserted in Agilent's preliminary injunction was not just obvious in view of the prior art, but actually ***anticipated***. *See* Ex. 2 at 29 ("Accordingly, based on the current record, Petitioner has established a reasonable likelihood it will prevail in demonstrating that claims 1–7, 9, 10, 12–15, 17, 18, 20–25, and 27–30 are anticipated by Pioneer Hi-Bred."); Ex. 1 at 30 (same). The PTAB notably found that this anticipation ground that applies to all the claims in Agilent's preliminary injunction motion was "particularly strong:"

> On the current record, we determine that the merits of Petitioner's anticipation ground appear to be ***particularly strong*** for the independent claims and for those dependent claims where Petitioner's arguments are similarly premised on the crRNA examples in Table 8 being anticipatory without any further modification.

Ex. 1 at 18; Ex. 2 at 18 (same).

The Board thoroughly considered and rejected each of Agilent's arguments on the merits, which were that the prior art failed to teach "gRNA functionality" and failed to enable. *See, e.g.*, Ex. 2 at 26 (identifying several examples of disclosure of "gRNA functionality" in the prior art and concluding that "Patent Owner's first argument is unavailing on the current record"); *id.* at 27-28 (finding that "Patent Owner's Preliminary Response does not identify evidence sufficient to overcome the presumption the SEQ ID NO: 64 and 65 example and the SEQ ID NOs: 66 and 67 example are enabling" and concluding that Agilent's enablement argument was "unavailing"). Agilent argued at length that the prior art was deficient because it lacked test data. The PTAB, however, rejected this, making clear that to "the extent Patent Owner suggests that test data confirming the 'gRNA functionality' of these examples is necessary for Pioneer Hi-Bred to be enabling prior art, we are skeptical that position is consistent with precedent." *Id.* at 28. The PTAB's three judge panel identified multiple Federal Circuit positions contrary to Agilent's position. *Id*.

Having reviewed Synthego's IPRs and Agilent's best responses on the merits, three PTAB judges concluded that there is a reasonable likelihood that Agilent's patents are invalid. In such circumstances, there is a clear question as to invalidity that precludes injunctive relief. *See, e.g.*, *Adidas Am., Inc. v. Sketchers USA, Inc.*, No. 3:16-cv-1400-SI, 2017 WL 2604310, at *6 (D. Or. June 12, 2017) ("Thus, based on the PTAB's instituting IPR on the pending [IPR Petitions], [Patent Owner] cannot, at this time, show a likelihood of success on the merits."); *Murata Mach. USA, Inc. v. Daifuku Co.*, Ltd., No. 2:13-CV-866-DAK, 2016 WL 4287040, at *2 (D. Utah Aug. 15, 2016) ("As long as the IPRs are pending before the Patent Trial and Appeals Board, the court concludes that [Patent Owner] will not be able to demonstrate a likelihood of success on the merits."); *see also Waters*, 410 F.Supp.3d at 713 (denying preliminary injunction because in "view of the obviousness challenge presented by Defendant and the response of Plaintiffs, the Court finds that there are difficult questions relating to obviousness of claim 6 of the '234 Patent on both sides").

b. Agilent's Expert And Technical Documents Confirm Invalidity

While Agilent's failure to provide a persuasive response to the substance of Synthego's IPRs and the PTAB's concomitant institution decisions are reason enough to find that Agilent has no likelihood of success, the invalidity of Agilent's patents is further borne out by its expert's admissions

and Agilent's internal documents, none of which has been put before the PTAB and that presents an independent basis establishing that injunctive relief is not warranted.

Agilent's expert witness, Dr. William Marshall, opined that that there had been a well-known issue with using RNA as a therapeutic drug, which is that "when guide RNA with unmodified ribonucleotides is introduced into the cellular matrix, and when introduced into mammalian cells in particular, it will be in the presence of native cellular exonucleases, which will begin to degrade the RNA, resulting in a non-functional … system." Dkt. No. 42 ¶¶ 54-55. [redacted] *See* Ex. 5 at 63:17-65:1. The key prior art relied upon in Synthego's IPRs, Pioneer Hi-Bred, likewise identifies precisely this issue:

> Nucleic acids expressed or delivered transiently to cells are subject to turnover or degradation. To increase the effective lifespan or stability of the nucleic acid component(s) of the guide polynucleotide/Cas endonuclease system in vivo, nucleotide and/or phosphodiester bond modifications may be introduced to reduce unwanted degradation. Examples of nuclease resistant nucleotide and phosphodiester bond modifications are shown in Table 7 and may be introduced in any one of the VT and/or CER domains of the guide polynucleotide.

Ex. 6 at 106.

While the problem of RNA degradation had long been known, the ***solution*** had also been known for decades. [redacted]. Ex. 5 at 69:13-21. [redacted] *Id.* at 70:1-10, 76:17-77:6. [redacted] *Id.* at 73:13-18, 76:17-77:6. [redacted] *Id.* at 81:19-25, 84:2-15. [redacted] *Id.* at 76:2-9, 79:15-22, 79:24-80:3, 84:1-21.

"Where the level of ordinary skill in the art is high, and the claim applies a known solution to a known problem, it is 'likely the product not of innovation but of ordinary skill and common sense.'" *Praxair Distribution, Inc. v. Mallinckrodt Hosp. Prod. IP Ltd.*, 890 F.3d 1024, 1037 (Fed. Cir. 2018) (internal citations omitted) (quoting *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 421 (2007)). This is the prototypical case involving patents that, at best, reflect nothing but the application of a tried-and-true technique to address a problem that had long been solved by that very technique.

Agilent's internal documents show this too. [redacted] *See* Ex. 7; Ex. 8 at 28:9-11. [redacted] *See Id.* at 23:3-24:10. 29:9-16. [redacted]

Ex. 7 at 1. [redacted] *See id.* ("[redacted]"); *id.* at 2 ("[redacted]").

As another example, [redacted] Ex. 9. [redacted] *See id.* at 3 ("[redacted]"); *id.* ("[redacted]"). Claiming nothing more than the "[redacted]" that was "[redacted]," Agilent's patents are invalid as obvious.

As a final example, with regard to the claimed 2'-O-methyl modification, [redacted]:

Ex. 10. [redacted]. *Id.* [redacted] Ex. 8 at 52:20-53:11; *see also id.* at 84:25-85:9 ("[redacted]").

Simply applying techniques for RNA stabilization that had long been known to make RNA "[redacted]" is not inventive, but rather obvious. As in the *Waters* case, the compelling evidence of obviousness from Agilent's expert and documents—none of which has yet been put before the PTAB—weighs against issuance of a preliminary injunction. *Waters*, 410 F.Supp.3d at 713 ("That each side makes compelling arguments renders this Court unable to find that Defendant's obviousness challenge lacks substantial merit, thus weighing against issuance of a preliminary injunction.").

2. The Asserted Patents Are Unenforceable

Another substantial question is raised by Synthego's showing regarding the unenforceability of the patents-in-suit, which may well render this case exceptional under § 285. As set forth in Synthego's pleading, the Agilent inventors inexplicably failed to disclose the Deleavey and Eckstein references during prosecution, even though, as they admitted in the Hendel paper, these very references were the source of the key modifications claimed in their patents. *See* Dkt. No. 24 at 13-16. Nevertheless,

according to Agilent, the "minimal allegations made by Synthego to date on inequitable conduct provide little indication that it will be able to muster the necessary evidence during discovery" to prove inequitable conduct. Dkt. No. 39-3 at 20. In fact, just the opposite is true. After only limited discovery in connection with this motion, including from Agilent's 30(b)(6) witness, there is proof of an inexcusable failure to disclose here.[2]

[redacted] *See* Ex. 8 at 70:19-72:18. [redacted] *Id.* at 41:4-42:1. [redacted] *Id.* at 47:7-48:9. [redacted] *Id.* at 75:2-77:9. [redacted]

Q. [redacted]

A. [redacted]

Q. [redacted]

A. [redacted]

Ex. 8 at 79:10-18. The most plausible explanation is that Agilent sought to deceive the Patent Office by withholding prior art that would have made abundantly clear that its alleged invention is obvious.

[2] Agilent also claims that Synthego's inequitable conduct claims are "doomed" because Deleavey and Eckstein "were in fact disclosed." Dkt. No. 39-3 at 20. This is false. Agilent's contention that it disclosed Deleavey and Eckstein is based on the misstatement that Agilent satisfied its duty of disclosure by not actually submitting Deleavey and Eckstein, but by submitting the non-prior art Hendel paper, which merely cites Deleavey and Eckstein. As Synthego explained in its opposition to Agilent's motion to dismiss, this does not fulfill a patentee's duty of disclosure. *See* Dkt. No. 50 at 6-9; *California Inst. of Tech. v. Hughes Commc'n Inc.*, No. 2:13-cv-07245-MRP-JEM, 2015 WL 11089495 (C.D. Cal. May 5, 2015).

3. Synthego's Sales Outside Of The Research Market Do Not Infringe Because They Are Covered By The Safe Harbor Under § 271(e)

As documented below, Agilent has offered Synthego and several other entities a license to sell products for research activities. *See infra* Part B. Agilent has thus admitted that whatever harm such sales might cause would be compensable by normal monetary damages. *Id.* As such, Synthego's sales for research cannot be the basis for injunctive relief.

Whatever additional sales Synthego currently has also cannot be the basis for injunctive relief because, even to the extent Agilent contends they are outside the scope of the research license that Agilent offered to Synthego, there is at least a substantial question as to whether these sales are covered by the safe harbor of 35 U.S.C. § 271(e)(1), which provides that it is not "an act of [patent] infringement to…use…or import into the United States a patented invention…solely for uses reasonably related to the development and submission of information under a Federal law which regulates the…use of drugs." 35 U.S.C. § 271(e)(1). This so-called "safe harbor" statute "provides a wide berth" for the use of patented inventions in activities related to the federal regulatory process. *Merck KGaA v. Integra Lifesciences I, Ltd.*, 545 U.S. 193, 202 (2005).

Indeed, § 271(e)(1) "extends to ***all uses*** of patented inventions that are ***reasonably related*** to the development and submission of any information [to the FDA]." *Id*. It also includes any activity "where a drugmaker has a reasonable basis for believing test that a patented compound may work...[and], if successful, would be appropriate to include in a submission to the FDA." *Id*. at 207. Included in the exemption are cases where work relating to the patented compound ultimately fails. The safe harbor exemption applies even if an FDA application is never filed. *See id*. at 206 ("Congress did not limit § 271(e)(1)'s safe harbor to the development of information for inclusion in a submission to the FDA…"). Importantly, the safe harbor provision covers not only the entities who are directly involved in FDA submissions but also entities, such as Synthego, who supply drug makers with material for use in obtaining FDA approval, including compounds used as part of therapeutics. *See Shire LLC v. Amneal Pharms., LLC*, 802 F.3d 1301, 1310 (Fed. Cir. 2015) (supplier of active ingredient was covered by the § 271(e)(1) exemption).

As Synthego's Senior Director of Quality and Regulatory, Beckinam Nowatzke, explains, Synthego sells three grades of guide RNA: (1) research-grade, (2) GMP-like, and (3) GMP. Nowatzke Decl. ¶ 5. Research grade is for pure scientific research activities, and, as noted above, cannot be the basis for injunctive relief given Agilent's willingness to freely license such uses. *Id.* GMP-like RNA is for customers seeking higher quality product with additional quality-related documentation, but who do not require products manufactured in accordance with the full set of "good manufacturing practice" ("GMP") requirements promulgated by the FDA. *Id.* And, finally, GMP RNA is fully compliant with the FDA's good manufacturing practice requirements and is accompanied by documentation consisting of a certificate of conformance, certificate of analysis, and customer-approved batch records. *Id.*

Customers who purchase either GMP-like or GMP products are ***not*** engaged in pure research activities (*i.e.*, early stage research that is not for the purpose of generating data for an FDA submission); it would make no sense for a customer to go to the added trouble and expense of buying such reagents when the much cheaper research-grade reagents can be used. *See id.* ¶¶ 7, 21. Agilent insinuates in its brief that Synthego may be supplying such product for use in RNA-based drugs to treat patients, asserting that "the ultimate sale of an approved drug" is not covered by the safe harbor. Dkt. No. 39-3 at 17. Yet, as Ms. Nowatzke explains, nobody has been granted approval to market any CRISPR-based RNA therapeutic, let alone a therapeutic using Synthego's products. Nowatzke Decl. ¶¶ 9-10. None of Synthego's customers have procured such approval. *Id.* In fact, Synthego's product documentation prohibits uses for commercial therapeutic use and states that the products are for "investigational use only" and "not intended for use as drugs." *Id.* ¶¶ 10-11, 22-23, 25, 26, 31-34. Synthego's GMP-like and GMP products are ***not*** used in FDA-approved commercial therapeutics.

Used neither for pure research nor for FDA-approved commercial therapeutics, Synthego's GMP-like and GMP products are, in fact, used in connection with clinical studies for the purpose of seeking FDA approval (whether of an Investigational New Drug to enable clinical trials or to provide data in support of an new drug application or biologics license application submission), which is covered by the safe harbor. As Ms. Nowatzke explains, the "investigational use only" label associated with these grades of product is a "term of art in the field that means the product is to be used in connection with clinical research reasonably related to the submission of information to the FDA, but

not commercial therapeutic uses." *Id.* ¶¶ 24, 32. The terms of sale associated with the GMP-like and GMP products expressly require that the customer represent that the products will be used "solely for uses reasonably related to the development and submission of information under a federal law which regulates the manufacture, use or sale of drugs or veterinary biological products." *Id.* ¶¶ 23, 33.

As Ms. Nowatzke explains, "when existing and prospective customers approach Synthego for quotes on GMP-like or GMP material, Synthego will ask the customer for the purpose of their purchase and how the materials will be used. Synthego requires this information because the customer's intended use of the Synthego product determines the type of release testing and documentation required for the material." *Id.* ¶ 13. Accordingly, Synthego is aware that its customers for GMP-like and GMP are using them for work related to the submission of information to the FDA, as is fully consistent with Synthego's product labeling and terms of sale. *Id.* ¶¶ 26, 34. In fact, Ms. Nowatzke has personally consulted with several of these customers on the preparation of investigational new drug applications for submission to the FDA. *See id.*

Agilent cannot credibly dispute that this is how Synthego's products will be used by its customers because Agilent also structures its RNA products in three tranches that exactly parallel Synthego's product grades. While both Agilent and Synthego sell RUO grade products, Agilent's Associate V.P. of Strategy and Marketing, Gary Carter, further described Agilent as selling "clinical grade" products that correspond to Synthego's GMP-like products and that enable "the evaluation of therapeutic modalities" in a "mid-scale" market. Dkt. No. 43 ¶ 4, 6. Customers who purchase such products, Dr. Carter explains, "are exploring the possibility of developing a human therapeutic." *Id.* ¶ 6. [redacted]

Q. [redacted]

A. [redacted]

Q. [redacted]

A. [redacted]

Ex. 11 at 127:22-128:9. Just as Agilent's mid-scale products are for purposes that fall within the safe harbor, so too are Synthego's GMP-like products.

And, just as Synthego sells a fully GMP compliant grade of products that are used to develop data for seeking FDA approval, so too does Agilent. *See* Dkt. No. 43 ¶ 7. As Mr. Carter explained, the fully GMP-compliant grade of product is for customers "who have reached the stage of conducting clinical trials of a potential new human therapeutic and are using gRNA in connection with those trials." *Id*.

Thus, to the extent Agilent pins its hopes of an injunction on the sales of Synthego's GMP-like and GMP products, it will not be able to prove infringement because all sales of these products are covered by the safe harbor.

B. Agilent Has Not Established That It Will Suffer Irreparable Harm Absent A Preliminary Injunction

Agilent also fails to meet its burden to prove it will incur irreparable harm absent a preliminary injunction. Agilent's irreparable harm argument is inconsistent with its lack of diligence, disproven by its desire to broadly license its patents, and all-around at odds with the record.

1. Agilent Did Not Bring Its Preliminary Injunction Motion With Reasonable Diligence

It is hornbook law that "a party requesting a preliminary injunction must generally show reasonable diligence." *Benisek v. Lamone*, 138 S.Ct. 1942, 1944 (2018) (per curiam). Agilent successfully opposed a preliminary injunction motion recently based upon undue delay. *Waters*, 410 F.Supp.3d at 714-15 ("Injunctive relief has been found to be inappropriate where a Plaintiff has had no apparent urgency in requesting it."). The delay Agilent complained about in *Waters* was much less than that here and involved only a matter of months. *Id.* ("If imminent and irreparable harm was expected, Plaintiffs certainly could have and should have moved with greater dispatch. The delay in asserting the '234 Patent cuts against a notion that the availability and sale of InstantPC is creating an irreparable harm to Waters.").

In *Waters,* Agilent successfully explained how little tolerance courts have for delay in bringing a preliminary injunction motion:

> Injunctive relief is not appropriate when there is no apparent urgency in requesting it. See, *High Tech. Med. Instrumentation, Inc. v. New Image Indus., Inc.,* 49 F.3d 1551, 1557 (Fed.

> Cir. 1995); *see also Hybritech Inc. v. Abbott Labs.*, 849 F.2d 1446, 1457 (Fed. Cir. 1988). ***In most cases, a mere matter of days or months constitutes undue delay.*** *See, e.g.*, *High Tech. Med.*, 49 F.3d at 1557 (17-month delay); *Agrofresh, Inc. v. Hazel Tech., Inc.*, No. 18-1486-MN, Slip Op. at 8 (D.Del. Oct. 12, 2018) (18-day delay "significant" given the timing); *Power Integrations, Inc. v. BCD Semiconductor, Corp.*, No. CIV. 07-633-JJF/LPS, 2008 WL 5069784,at *12 (D. Del. Nov. 19, 2008) (three-month delay); *Neology, Inc. v. Fed. Signal Corp.*, No. 11-672-LPS/MPT, 2012 WL 2308202, at *17 (D. Del. June 18, 2012) (seven-month delay).

Ex. 12 at 10 ("Waters waited for over fifteen months from when the '234 Patent issued").

Here, the delay is extensive and inexcusable, especially because Agilent was well-aware of how little tolerance there is for delay in bringing a preliminary injunction motion in view of the *Waters* case. Synthego's accused products have been offered since 2016. Steiner Decl. ¶ 4.

Agilent's '001 Patent asserted in this action issued ***three years*** ago in July 2019. [redacted] Ex. 11 at 88:8-12. [redacted] *Id.* 52:21-53:5 ([redacted]); *id.* at 55:7-12 ([redacted]). [redacted] *Id.* at 62:2-10. [redacted] *Id.* at 61:8-13 ([redacted]). [redacted] warrants denial of this motion.

[redacted] Ex. 13 at. 76:1-12. [redacted] Ex. 11 at 77:10-20 ([redacted]).

[redacted]

[redacted] Ex. 13 at 77:10-16. [redacted]

[redacted]

[redacted]

Q. [redacted]

A. [redacted]

Q. [redacted]

A. [redacted]

Id. at 83:13-22; *id.* at 84:13-16 (same).

From June 2021 until October 5, 2021, Agilent sent emails to Synthego about its patents, including threatening legal action, but did not actually follow through. Accordingly, on October 5, 2021, Synthego brought this declaratory judgment action to address Agilent's belated licensing threats. It took another three months for Agilent to bring this motion.

Agilent's lackadaisical pace in its patent assertion attempts is not limited to its approach to Synthego. [redacted] Ex. 11 at 66:1-4. [redacted]. Ex. 13 at 75:11-16. [redacted]

[redacted]

[redacted]

[redacted] Ex. 13 at 113:6-22.

Agilent's excuse in its motion for its lack of diligence is empty. First, Agilent argues that it was waiting for its second patent to issue. Dkt. No. 39-3 at 23:20-22. [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]. And even if Agilent's witnesses had tried to back up Agilent's argument, Agilent has not

explained what it is about the '034 Patent that would possibly justify that delay. Second, Agilent argues that it filed this motion within three months of Synthego bringing this action. *Id.* at 23:23-24:1. Leaving aside whether that was reasonable, that three month delay does not excuse the multi-year delay from July 2019 until January 2022.

In sum, Agilent delayed asserting its patents for two and half years from when it first believed Synthego infringed and has not offered any plausible, much less good, excuse. Because there is no reasonable diligence, the motion should be rejected.

2. Agilent's Desire To License The Industry Proves That Any Harm Is Monetarily Compensable

In *Cave Consulting Grp., LLC v. Optuminsight, Inc.*, No. 5:11-cv-00469-EJD, 2016 WL 4658979, at *21 (N.D. Cal. Sept. 7, 2016), because of the patentee's licensing practices, this Court held that there was no irreparable harm and denied an injunction. This Court explained that a "patent holder's 'willingness to forego its patent rights for compensation supports the...conclusion that [the patent holder] will not suffer irreparable harm absent an injunction.'" *Id.* (*citing Advanced Cardiovascular Sys., Inc. v. Medtronic Vascular, Inc.*, 579 F.Supp.2d 554, 560 (D. Del. 2008)). "Money damages are rarely inadequate in these circumstances." *Id.* On very similar facts, this Court stated that "CCGroup has been willing to license the '126 Patent to Optum and other competitors. 'As a general rule, courts will find that monetary damages are sufficient in such cases.' *Advanced Cardiovascular Sys., Inc. v. Medtronic, Inc.*, No. C95- -03577, 2008 WL 4647384, at *10 (N.D. Cal. Oct. 20, 2008)." *Id.*

This has long been the governing law. *See, e.g.*, *High Tech Med. Instrumentation, Inc. v. New Image Indus., Inc.,* 49 F.3d 1551, 1557 (Fed. Cir. 1995) (Because Plaintiff "offered a license to [Defendant], [] it is clear that [Plaintiff] is willing to forgo its patent rights for compensation. That evidence suggests that any injury suffered by [Plaintiff] would be compensable in damages assessed as part of the final judgment in the case.").

Here, Agilent has set up licensing programs that have been unsuccessful, but not for lack of trying. [redacted] Ex. 11 at 66:22-23 [redacted] Ex. 13 at 21:22-22:2, 34:6-15, 35:15-25, 40:23-41:25, 61:11-19,

72:22-73:3. In that sector, there is no irreparable harm because Agilent wants to trade its patent rights for royalties. Agilent does not meaningfully dispute this.

For the therapeutic (high-grade "GMP") market sector, Agilent also has been attempting to license the patents-in-suit widely. [redacted] Ex. 11 at 68:8-22 [redacted] *Id.* 70:3-71:8. [redacted] Ex. 13 at 66:14-23, 28:15-29:6, 67:23-68:6. [redacted] *Id.* at 70:17-23 [redacted] *Id* at 40:7-12, 43:7-12.

Agilent recognizes the general principle that licensing is inconsistent with an injunction, but tries to find an exception based on the "restriction" from the therapeutics and diagnostics (GMP) field. Dkt. No. 39-3 at 22:20-23:19. This argument fails to defend the injunction as it relates to everything except the GMP products. For all other products, including the RUO field, there is no irreparable harm showing even accepting Agilent's limited licensing argument about GMP restrictions. Moreover, as explained above, Agilent in fact offers licenses for the GMP field and has no policy against licensing gRNA vendors for GMP products. All of this conduct is inconsistent with Agilent's irreparable harm argument and is another independent ground to deny this motion.

3. Agilent's Irreparable Harm Arguments Conflict With The Law And The Record

Agilent's leading irreparable harm argument is that Agilent and Synthego compete directly and "[e]very sale of a gRNA product made by Synthego is therefore a lost sale to Agilent." Dkt. No. 39-3 at 21:2-7. This assertion is flatly inconsistent with the record.

As the *Waters* court recently explained at Agilent's behest, mere allegations of lost sales, especially if based on speculation, are insufficient to justify a preliminary injunction:

> The Federal Circuit has found that "lost sales standing alone are insufficient to prove irreparable harm; if they were, irreparable harm would be found in every case involving a 'manufacturer/patentee, regardless of circumstances.'"*Automated Merchandising Sys., Inc. v. Crane Co*., 357 Fed. App'x 297, 300-01 (Fed. Cir. 2009).
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> The Federal Circuit has found "lost market share must be proven (or at least substantiated with some evidence) in order for it to support entry of a preliminary injunction, because granting preliminary injunctions on the basis of speculative loss of market share would result in granting preliminary injunctions 'in every patent case where the patentee practices the invention.'" *Automated Merchandising Sys.,* 357 Fed. App'x at 301 (citing *Nutrition 21 v. United States*, 930 F.2d 867, 871 (Fed. Cir. 1991)).

Waters v. Agilent, 410 F. Supp. 3d at 714-15.

Agilent's factual showing is weak. [redacted]. Ex. 11 at 88:2-7. [redacted]. *Id.* at 32:3-13. [redacted] *Id.* This alone establishes Agilent cannot carry its burden.

An analysis of each of the three market sectors described by Agilent also confirms there is no irreparable harm. That is followed by an analysis of Agilent's arguments about price and KOLs.

a. RUO Market Sector

Agilent is not a substantial participant in the RUO market sector, which focuses on small volumes of gRNA for researchers. [redacted]

[redacted] Ex. 11 at 104:8-22 ("[redacted]"). But the "moving party must demonstrate that immediate irreparable harm is likely in the absence of injunctive relief—not merely that irreparable harm may possibly occur at some point in the future." *Waters*, 410 F. Supp. 3d at 713.

[redacted]. Ex. 11 at 15:8-21. [redacted]. *Id.* at 27:9-17; 29:11-30:4. [redacted] *Id.* at 86:16-87:3.

[redacted], *id.* at 32:13-16, [redacted], there is no showing of irreparable harm.

Any question about whether Agilent has shown irreparable harm in the RUO sector is extinguished by the declaration of Jason Steiner, Synthego's former Chief Strategy Officer. [redacted]. Steiner Decl. ¶¶ 6-8. [redacted] *Id.* He also explains that Agilent's focus is not on the "high volume, low quantity custom orders that are necessary for the RUO market segment." *Id.*

b. Midscale Market Sector

The midscale market includes preclinical sales and the larger sales for research use. [redacted]

[redacted] Ex. 11 at 15:25-16:15, 121:1-7. [redacted] *Id.* at 26:3-7. [redacted] *Id.* at 17:25-18:9. [redacted] *Id.* at 26:14-17. [redacted] *Id.* at 26:18-27:3 ("[redacted]"); *id.* at 30:6-10. [redacted] . *Id.*at 32:3-6 ("[redacted]"). This precludes a showing of irreparable harm.

Dr. Steiner identified a host of competitors in the midscale sector, including IDT, Trilink, Genscript, and LGC Biosearch/Axolabs. Steiner Decl. ¶ 10. He also explained that, for reasons similar to the RUO market, "Synthego generally does not compete with Agilent in the mid-scale market with respect to larger-scale RUO applications." *Id.*

In addition, the preclinical sector is generally protected by the safe harbor and thus not infringing anyway based on Mr. Carter's testimony. [redacted] Ex. 11 at 127:22-25; *see also UCB, Inc. v. Catalent Pharma Sols., Inc.*, No. 5:21-CV-00038-GFVT, 2021 WL 1910079, at *4 (E.D. Ky. May 12, 2021) (finding patentee "has not only failed to show the prospect of irreparable harm, but has shown no harm at all" where the alleged infringement was lawful under the Safe Harbor provision).

c. Clincial/GMP Market Sector

[redacted] Ex. 11 at 18:11-16, 23:6-13, 30:12-16. [redacted] *Id.* at 23:15-24:3. ("[redacted]"). [redacted] *Id.* at 25:5-13.

[redacted] *Id.* 32:7-11. This precludes a showing of irreparable harm. Dr. Steiner likewise explains that there are many competitors in this market sector including Biospring, LGC Biosearch/Axolabs, Genscript, Nitto Denko Avecia, and Trilink Biotechnologies. Steiner Decl. ¶ 10. [redacted] *Id.* ¶ 6. Moreover, as documented below, the GMP customers are performing pre-clinical and clinical studies for FDA approval and thus such sales are not infringing under the safe harbor.

d. Agilent's Arguments Regarding Price Are Unavailing

Agilent argues that Synthego causes irreparable harm by pricing gRNA lower than the market price. This argument is off-base. As this Court has explained: "Lost customers or lowered prices, if proven to be true, are forms of quantifiable harm compensable by money damages." *Cave Consulting*, 2016 WL 4658979 at *21. But even if Agilent's pricing argument was legally viable, it fails factually.

Agilent's attempt to paint Synthego as some sort of low-price outlier fails. [redacted] Ex. 11 at134:10-23. [redacted] *Id.* This is bad math. Using Mr. Carter's own numbers Synthego is $63 per nanomole, but GenScript is $49.5 per nanomole, which is substantially lower. Comparing price without accounting for a volume difference is meritless.

Even though, according to Agilent's numbers, GenScript, not Synthego, is the least expensive competitor, this motion would do nothing to remove them from the market. This underlines that Synthego's removal from the market would not avoid any price-based irreparable harm, even if Agilent had shown that Agilent and Synthego compete directly. [redacted] Ex. 14 at 44.

Agilent also criticizes Synthego for offering free sample gRNA products to customers. [redacted] Ex. 11 at 130:16-131:8. [redacted] Steiner Decl. ¶ 18. [redacted]

[redacted] *Id.* [redacted]

[redacted] *Id.*

e. Agilent's KOL Argument Is Unavailing

Agilent alleges that Synthego has recruited Agilent KOL's, creating a risk of irreparable harm. The only KOL identified by Agilent that switched to Synthego is Dr. Porteus, when in fact Dr. Porteus was using TriLink supplied gRNA before switching to Synthego. [redacted] Ex. 11 at 124:8-15.

Agilent's KOL complaint is stale and misguided. [redacted] Steiner Decl. ¶ 13. [redacted] *Id.*

4. The Balance Of The Harms Counsels Against An Injunction

Agilent's unjustified multi-year delay in pursuing this motion tilts the equities against an injunction. *Cave Consulting*, 2016 WL 4658979 at *23 ("CCGroup delayed in seeking an injunction for nearly five years, during which time Optum made investments in the product."). [redacted] Steiner Decl. ¶ 20.

As explained above, Agilent has not shown that it will incur non-compensable harm from Synthego's participation in the market. Agilent does not contend Synthego is a major competitor and there are many other participants in the marketplace. Agilent admits evidence of lost sales is speculative. On the other hand, Synthego has built a business on the accused products and the injunction Agilent seeks would prevent important sales. The balance of the harms tilts against an injunction.

5. The Public Interest Favors Denial Of An Injunction

As proven above, the only Synthego sales that Agilent could even conceivably contend cause it harm are those of the GMP-like and GMP grades of product that Synthego sells to companies engaged in clinical research. *See supra* Part III.A.3. Such sales, however, are not infringing pursuant to the safe harbor of 35 U.S.C. § 271(e)(1), and thus cannot be the basis for injunctive relief under any circumstances. *Id.*

They also cannot be the basis for injunctive relief for the additional reason that, if such sales for drug development were to be blocked, the public interest would be greatly harmed, according to Agilent's position in the *Waters* case. There, Agilent argued that denial of an "injunction is warranted because it would remove a product that is used in the critical pathway for biologic drug development and FDA submission." Ex. 12 at 19. The Court in *Waters* explained that "there is a strong countervailing public interest in allowing [Agilent's] products to remain available for drug development and regulatory approval." *Waters*, 410 F.Supp. 3d at 718. "[F]or good reason, courts have refused to permanently enjoin activities that would injure the public health." *Cordis Corp. v. Bos. Sci. Corp.*, 99 F. App'x 928, 935 (Fed. Cir. 2004). On the basis of Agilent's position in *Waters* alone, public interest considerations weigh against an injunction.

The Court in *Waters* further noted Agilent's argument that "an injunction would create a shortfall" in the ability of the relevant reagents for use in drug development. Exactly the same thing is true here. As Dr. Steiner explains, Synthego products are used in connection with clinical trials and there is a shortage of suppliers of gRNA for CRISPR applications who can serve the clinical trial market, a concern that has been exacerbated because several manufacturers have shifted their production efforts to supply components for mRNA-based vaccines. *See* Steiner Decl. ¶ 16.

In its brief, Agilent devotes only a few lines to the public interest, stating only that protecting patent rights "promotes innovation in the field of public biotechnology," and that if Synthego were enjoined the public supposedly could still obtain product from Agilent. Dkt. No. 39 at 25. As to the first point, however, Agilent made clear in *Waters* that on the facts here the public interest would be harmed from an injunction notwithstanding any countervailing interest in protecting patent rights. As to the second point, Agilent provides no evidence that Agilent could fill the demand for Synthego products except a single conclusory statement from Dr. Carter that Synthego and Agilent sell in the same markets. *See* Dkt. No. 43 ¶ 8. [redacted]. *See* Steiner Decl. ¶¶ 6-12. Following Agilent's own arguments in the *Waters* case, public interest considerations weigh against injunctive relief.

IV. CONCLUSION

For the foregoing reasons, Agilent's motion for a preliminary injunction should be denied.

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Respectfully submitted,

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